REMARKS/ ARGUMENTS

Applicants note with appreciation the detail and thoroughness embodied in Paper No. 20060906 and the opportunity to distinguish the pending claims over the prior art of record. This amendment is submitted to be fully responsive thereto. Claims 8-24, 26, 27, and 30 are currently pending in this application; claims 8-24, 26, 27, and 30 are presently under consideration. By way of this amendment, claims 8 and 20 have been amended. Claim 18 has been canceled.

Currently the Specification is objected to under 35 U.S.C. 132(a) as introducing new matter into the disclosure.

Currently, claim 18 is objected to under 37 CRF 1.75(c) as being in improper dependent form on the basis of further limiting the subject matter of a previous claim. Claims 8-24, 26, 27 and 30 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 8, 10, 13-18, 20, 23, 24, 26, and 27 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Gebeyehu et al (US Patent 6,075,012). Claims 8, 13, 14, 17, 18, 20, 23, 24, and 26 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Stupp et al (US Patent 5,932,539). Claims 8 and 30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gebeyehu et al (US Patent 6,075,012). Claims 9 and 11 stand rejected under 36 U.S.C § 103(a) as being unpatentable over Gebeyehu et al (US Patent 6,075,012) in view of Perrie et al (J. Liposome Res. 12(1&2): 185-197, 2002). Claims 10-12, and 19 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Gebeyehu et al (US Patent 6,075,012) as applied to claims 8 and 30 in further view of Kitadai et al (Brit. J. Cancer 81(14): 647-653, 1999).

The objection of claim 18 under 37 CFR 1.75(c) as being of improper dependent from for failing to further limit the subject matter of a previous claim is moot in light of the cancellation of this claim.

Remarks Directed to the Objection of the
Specification Under 35 U.S.C. 132(a): New Matter

Withdrawal of the objections to the specification under 35 U.S.C. 132(a) is requested for at least the following reasons. The amendment filed July 17, 2006 included amendments to the specification in the paragraph beginning on line 19 of page 4 and the paragraph beginning on line 15 of page 9 that are fully supported by the original disclosure as follows.

Applicants respectfully suggest that the objection to the amendments of page 19 of the specification is meant by the examiner as an objection to amendments to the paragraph on page 4 of the application beginning on line 19. The subject application as filed taught "deficiencies illustratively include: . . . cancer [page 5, line 2], . . . clotting disorders [page 5, line 10], . . . bone diseases [page 5, line 15], . . . myasthenia gravis [page 5, line 17]." Further, the subject application as filed taught "clotting disorders, antithrombin-III, other proteases or protease inhibitors, clotting factor VIII." A person having ordinary skill in the art recognizes that "other proteases or protease inhibitors" comprises the proteases of the clotting cascade as well as the proteins and small molecule inhibitors of said clotting cascade based on the position of the statement "other proteases or protease inhibitors" as well as the knowledge that components of the clotting cascade comprise a chain of proteases whose activity is balanced by inhibitors to regulate the deposition of fibrin and the parallel cellular response to injury. (Rantoff, OD, (1994) The development of knowledge about haemostasis and thrombosis. In Haemostasis and

Thrombosis, A.L. Bloom, C.D. Forbes, D.P. Thomas, and E.G.D. Tuddenham, eds. (Edinburgh: Churchill Livingstone), pp. 3-28). Thus, the subject specification as filed disclosed the treatment of deficiencies in cancer, deficiencies in clotting factors, and deficiencies in bone diseases.

The amendment to the paragraph beginning on page 9, line 23 of the subject specification does not introduce new matter into the specification for at least the following reasons. Claim 1 as originally filed taught "R_1 is a cholesterol derivative; a C_8-C_{24} alkyl; C_8-C_{24} heteroatom substituted alkyl wherein the heteroatom is O, N, or S." As the court in *In re Gardner* explained, "an original claim, in itself constituted a description in the original disclosure equivalent in scope and identical in language to the total subject matter now being claimed. . . . Nothing more is necessary for compliance with the description requirement." 475 F.2d 1389, 1391 (CCPA 1973). Thus, as claim 1 as originally filed taught that "R_1 is a cholesterol derivative; a C_8-C_{24} alkyl; C_8-C_{24} heteroatom substituted alkyl wherein the heteroatom is O, N, or S," the amendment to the paragraph beginning on page 9, line 23 of the subject specification ~~does not~~ as such is submitted to not constitute new matter. Additionally, the insertion of "herteratom substituted" to modify C_8-C_{24} alkyls is submitted to be supported by and more accurately reflect the specific example of that paragraph.

For at least the above reasons, applicants respectfully request all objections to the specification under 35 U.S.C. 132(a) be withdrawn.

Remarks Directed to the Objection to
Claim 18 Under 37 CFR 1.75(c): Proper Dependent Form:

The objection to claim 18 under 37 CFR 1.75(c) is moot in light of the current cancellation of this claim.

Remarks Directed to the Rejection of Claim 8-24, 26, 27, and 30 Under 35 U.S.C. § 112, First Paragraph, Written Description:

Withdrawal of the rejection of claims 8-24, 26, 27, and 30 under 35 U.S.C. § 112, First Paragraph, Written Description, is respectfully requested for at least the following reasons. The claims contain subject matter described in the application as originally filed in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time of the application, had possession of the claimed invention.

The subject application as originally filed described A as "a hydrophilic moiety A that illustratively includes C_0-C_4 alkyl-hydroxy, -substituted amino, -quaternary amino, -sulfonate, -phosphonate, and –carboxylate; and targeting ligand; where the targeting ligand includes amino acids, hormones, antibodies, cell adhesion molecules, folate, polypeptides, vitamins, saccharides, transferrin, drugs, and neurotransmitters." (page 9, lines 18-23.) Further, the subject application described R_1 as "a cholesterol derivative; a C_8-C_{24} alkyl; C_8-C_{24} heteroatom substituted alkyl wherein the heteroatom is O, N, or S; or membrane importer and transporter proteins" in claim 1 as originally filed. (Claim 1.) The amendment to the paragraph beginning in page 9, line 15 has been previously amended to correct a typographical error and presently describes R_1 as "a cholesterol derivative; a C_8-C_{24} alkyl; C_8-C_{24} heteroatom substituted alkyl wherein the heteroatom is O, N or S" which is fully supported by the application as originally filed in claim 1. Thus, A is described independently of R_1. A claim as originally filed represents a portion of the written description. *In re Gardner*, 475 F.2d 1389, 1391 (CCPA 1973). Additionally, the "claims as filed in the original specification are part of the disclosure and, therefore, if an

application as originally filed contains a claim disclosing material not found in the remainder of the specification, the applicant may amend the specification to include the claimed subject matter." MPEP 2163; *In re Benno*, 768 F.2d 1340 (Fed. Cir.

1985). In light of the amendment the paragraph beginning on page 9, line 15 to correct an improper definition of A to coincide with the remainder of the written description, the application as filed supports embodiments of A as –sulfonate, -phosphonate, or targeting ligand groups and the claims do not recite new matter. An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also recognize the appropriate correction. *In re Oda*, 443 F.2d 1200 (CCPA 1971).

The claims presently define R_1 as adequately described in the application as filed. Claim 1 as originally filed taught "R_1 is a cholesterol derivative; a C_8-C_{24} alkyl; C_8-C_{24} heteroatom substituted alkyl wherein the heteroatom is O, N, or S." As the court in *In re Gardner* explained, "and original claim, in itself constituted a description in the original disclosure equivalent in scope and identical in language to the total subject matter now being claimed. . . . Nothing more is necessary for compliance with the description requirement." 475 F.2d 1389, 1391 (CCPA 1973). Thus, the claims as presented do not recite new matter.

Further, an embodiment comprising R1 as a bile acid was also present in the subject specification as filed. A preferred embodiment is described as "a nucleic acid conjugating agent contains a bile acid linked with a polycationic peptide." (page 3, lines 6-7.) Given that Z is described as a polyionic peptide (page 10, line 2) and Y is described as a linker peptide (page 10, line 1), a person having ordinary skill in the art recognizes that R1 is described as comprising a bile acid and was adequately described in the subject specification as of the filing date.

Therefore, all claims recite subject matter present in the application as of the filing date and do not contain new matter. For at least the above reasons, applicants respectively request the rejection of claims 8-24, 26, 27, and 30 under 35 U.S.C. § 112, First Paragraph, Written Description be withdrawn.

Remarks Directed to the Rejection of Claims 8, 10, 13-18, 20, 23, 24, 26 and 27 Under 35 U.S.C. § 102(b) as Anticipated by Gebeyehu et al (US Patent 6,075,012):

Withdrawal of the rejection of claims 8, 10, 13-18, 20, 23, 24, 26, and 27 under 35 U.S.C. § 102(b) as anticipated by Gebeyehu at al (US Patent 6,075,012) is respectfully requested in view of the proffered amendments to comport with subject matter currently under examination. In light of these amendments withdrawal of the outstanding claim rejection is respectfully requested. Gebeyehu et al. does not teach all elements of the claimed invention. Claims 8 and 20 are currently amended "**with the proviso that when A is the C_0-C_4 alkyl-hydroxy, Q is oxygen.**"

Gebeyehu et al. does not teach or suggest the invention of amended claim 8 in regard to the above quotation from that claim as well as other aspects, applicant reserves the right to make of record in due course. In contrast to pending independent claims 8 and 20, Gebeyehu et al was correctly construed by the Examiner (Paper No. 20060906, page 5) in the most relevant teaching as providing a linker "A" as -$NHCH_2$- when the adjacent "R" is cholic acid. Thus, Gebeyehu does not teach or suggest each and every element of independent claims 8 and 20 expressly or inherently and, thus, they are not anticipated. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Further, as claims 10 and 13-18 depend from claim 8 and claims 23, 24, 26, and 27 depend from claim 20, each of these dependent claims incorporate by reference the novel limitations of the claims from which they refer. Applicant submits that additional bases exist for the patentability of the claims dependent from claims 8 and 20, and reserves the right to later make these of record.

Finally, as the subject inventive compositions are not taught or suggested by Gebeyehu et al, the use of the claimed compositions alone or as a kit to transfect subject cells *in vivo* and *in vitro* for research purposes with DNA or RNA encoding expressible proteins of ribozymes, or are similarly neither taught nor contemplated by Gebeyehu et al.

In light of the above remarks, it is respectfully requested that the rejection of claims 8, 10, 13-18, 20, 23, 24, 26, and 27 under 35 U.S.C. § 102(b) as anticipated by Gebeyehu at al (US Patent 6,075,012) be withdrawn.

Remarks Directed to the Rejection of Claims 8, 13, 14, 17, 18, 20, 23, 24, and 26 Under 35 U.S.C. § 102(b) as Anticipated by Strupp et al (US Patent 5,932,539):

Withdrawal of the rejection of claims 8, 13, 14, 17, 18, 20, 23, 24, and 26 under 35 U.S.C. § 102(b) as anticipated by Stupp at al (US Patent 5,932,539) is respectfully requested in view of the proffered amendments to comport with subject matter currently under examination consistent with the election of record. In light of these amendments withdrawal of the outstanding claim rejection is respectfully requested. Stupp does not teach all limitations of the claimed invention.

In contrast to the claimed invention of independent claims 8 and 20 that have a hydrophilic moiety "A" extending from the R_1 as a terminal group to impart solubility to the inventive complex, Strupp et al. in every instance where cholesterol is used as the analog to

inventive group R_1, the hydroxyl group is deprotonated to form a linkage to the linker (such as 0-lactide) (see Figs 1 and 2; col. 3, lines 15-41; and examples of col. 7, line 56 – col. 11, line 57). Furthermore, Strupp et al. teaches that group L is a lipophilic group (column 2, line 57) and is distinguishable from the hydrophilicity imparted by claimed hydrophilic group "A".

Further, as claims 13, 14, 17, and 18 depend from claim 8 and claims 23, 24, and 26 depend from claim 20, each of these claims incorporate by reference the novel limitations of the claims from which they refer. Applicant submits that additional bases exist for the patentability of the claims dependent from claims 8 and 20, and reserves the right to later make these of record.

Therefore, Strupp does not anticipate embodiments of the instant claims requiring A-R_1-Q-Y-Z. In light of the above remarks, it is respectfully requested that the rejection of claims 8, 13, 14, 17, 18, 20, 23, 24, and 26 under 35 U.S.C. § 102(b) as anticipated by Stupp at al (US Patent 5,932,539) be withdrawn.

Remarks Directed to the Rejection of Claims 8 and 30 Under 35 U.S.C. § 103(a) as Being Unpatentable Over Gebeyehu et al (US Patent 6,075,012):

Withdrawal of the rejection of claims 8 and 30 under 35 U.S.C. § 103(a) as being unpatentable over Gebeyehu at al (US Patent 6,075,012) is respectfully requested in view of the proffered amendments to comport with subject matter currently under examination. In light of these amendments withdrawal of the outstanding claim rejection is respectfully requested. Gebeyehu does not teach or suggest all limitations of the claimed invention.

Claim 8 as currently amended "**with the proviso that when A is the C_0-C_4 alkyl-hydroxy, Q is oxygen.**" Thus, each and every element of claim 8 is not taught by Gebeyehu expressly or inherently. "To establish prima facie obviousness of a claimed invention, all the

claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

Gebeyehu et al. teaches away from delivery of DNA (col. 6, lines 37-38). As such, it is submitted that of ordinary skill in the art would not be motivated to even attempt the claimed method of nucleic acid delivery in light of this teaching. This in itself is strongly suggestive that the claimed methodology is non-obvious in view of Gebeyehu et al.

Gebeyehu et al also does not teach or suggest the composition in which the linker "A" in the R-A-Z parlance of Gebeyehu et al. is oxygen when "R" is cholic acid. In deed, Gebeyehu et al. only teaches a linker chemistry involving nitrogen (col 29, scheme 8). The R group of Gebeyehu et al. is taught only to be a C1-23 alkyl or alkenyl, or a steroid selected from the group consisting of stigmasterol, ergosterol and cholic acid. (col. 3, lines 61-64.) Additionally, there is no motivation taught in Gebeyehu et al. for invoking completely different linker chemistry.

Furthermore, as Gebeyehu does not teach or suggest the subject inventive compositions of dependent claim 30, the reference also does not teach or suggest a commercial package comprising A-R_1-Q-Z as an active ingredient together with instruction for the use thereof as a nucleic acid delivery agent to a subject.

In light of the above remarks, applicants respectfully request that the rejection of claims 8 and 30 under 35 U.S.C. § 103(a) as being unpatentable over Gebeyehu at al (US Patent 6,075,012) be withdrawn.

Remarks Directed to the Rejection of Claims 9 and 11 Under 35 U.S.C. § 103(a) as Being Unpatentable Over Gebeyehu et al (US Patent 6,075,012) in View of Perrie et al (J. Liposome Res. 12(1&2): 185-197, 2002) and Gebeyehu et al (US Patent 6,075,012) in View of Kitadai et al (Brit. J. Cancer 81(14): 647-653, 1999):

Withdrawal of the rejections of claims 9 and 11 under 35 U.S.C. § 103(a) as being unpatentable over Gebeyehu at al (US Patent 6,075,012) in view of Perrie et al (J. Liposome Res. 12(1&2): 185-197, 2002), and the rejection of claims 10-12 and 19 under 35 U.S.C. § 103(a) as being unpatentable over Gebeyehu at al (US Patent 6,075,012) in view of Kitadai et al (Brit. J. Cancer 81(14): 647-653, 1999) is respectfully requested in view of the proffered amendments to comport with subject matter currently under examination. In light of these amendments withdrawal of the outstanding claim rejection is respectfully requested. Neither Gebeyehu in view of Perrie et al., nor Gebeyehu et al. in view or Kigadai et al teach or suggest all limitations of the claimed invention individually, or combined in any manner.

As described above, Gebeyehu not only does not teach or suggest all the limitations of the subject claimed invention, but teaches away from nucleic acid delivery through the exclusion of DNA (col. 6, lines 37-38); combinations of elements in Gebeyehu et al. fail to yield the subject claimed invention.

Perrie et al. is limited to teaching oral administration of a liposome entrapped plasmid DNA molecule. This route of administration is distinct from both Gebeyehu et al. and the subject application. Perrie teaches that protection of the DNA by entrapment into liposomes is essential to its protection, (p. 186, Introduction; p. 190), and that surface expression of the DNA leads to degradation by nucleases (p. 193). However, as Gebeyehu et al. teaches away from DNA delivery, and as such contraindicates the proposed prior art reference combination.

As the subject inventive compounds are distinguishable from and are not taught or suggested by Gebeyehu et al., Perrie et al., or Kitadai et al. alone or in combination, they are not equivalents. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on Applicant's

disclosure or the mere fact that the components at issue are functional or mechanical equivalents. MPEP 2144.06; *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958). One or ordinary skill in the art would not consider the prior art reference combination since Gebeyehu et al precludes DNA delivery. As such the prime facie case of obvious is respectfully submitted to have been rebutted.

Likewise, it would not be obvious to a person having ordinary skill in the art to substitute the subject inventive compounds in the method of Kitadai et al. on the basis of Gebeyehu et al. teaching away from such as combination for DNA delivery, as detailed above. Kitadai et al. uses the cationic lipid formulation Lipofectin to facilitate transfection of cells. The DNA is inserted into the cells after being packaged into micelles of Lipofectin. Gebehehu et al. teaches away from the compounds disclosed therein being suitable for DNA delivery as per the Lipofectin of Kitadai et al.

In light of the above remarks, withdrawal of the rejections of claims 9 and 11 under 35 U.S.C. § 103(a) as being unpatentable over Gebeyehu at al (US Patent 6,075,012) in view of Perrie et al (J. Liposome Res. 12(1&2): 185-197, 2002), and the rejection of claims 10-12 and 19 under 35 U.S.C. § 103(a) as being unpatentable over Gebeyehu at al (US Patent 6,075,012) in view of Kitadai et al (Brit. J. Cancer 81(14): 647-653, 1999) is respectfully requested.

SUMMARY

Claims 8-24, 26, 27, and 30 are currently pending in this application. Applicant submits that claims 8-24, 26, 27, and 30 are now in allowable form and directed to patentable subject matter. Reconsideration and allowance of the pending claims is solicited. Should the Examiner

have any suggestions as to how to improve the form of the pending claims, he is respectfully requested to contact the undersigned attorney in charge of this application.

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Respectfully submitted,

By /Avery N. Goldstein, Ph.D./
Avery N. Goldstein, Ph.D.
Registration No.: 39,204
GIFFORD, KRASS, GROH, SPRINKLE,
ANDERSON & CITKOWSKI, P.C.
2701 Troy Center Drive, Suite 330
Post Office Box 7021
Troy, Michigan 48007-7021
(248) 647-6000

Attorney for Applicant